

PATENT COOPERATION TREATY

From the
INTERNATIONAL SEARCHING AUTHORITY

PCT

WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

<p>To: PATRICK J. HAGAN DANN DORFMAN HERRELL AND SKILLMAN 1601 MARKET STREET SUITE 2400 PHILADELPHIA, PA 19103-2307</p>		<p>Date of mailing (day/month/year) 09 DEC 2004</p>
<p>Applicant's or agent's file reference SAR15036PCT</p>		<p>FOR FURTHER ACTION See paragraph 2 below</p>
<p>International application No. PCT/US04/02142</p>	<p>International filing date (day/month/year) 26 January 2004 (26.01.2004)</p>	<p>Priority date (day/month/year) 27 January 2003 (27.01.2003)</p>
<p>International Patent Classification (IPC) or both national classification and IPC IPC(7): A61K 9/22 and US Cl.: 604/890.1</p>		
<p>Applicant SARNOFF CORPORATION</p>		

1. This opinion contains indications relating to the following items:

- Box No. I Basis of the opinion
- Box No. II Priority
- Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- Box No. IV Lack of unity of invention
- Box No. V Reasoned statement under Rule 43bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- Box No. VI Certain documents cited
- Box No. VII Certain defects in the international application
- Box No. VIII Certain observations on the international application

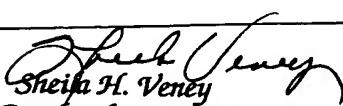
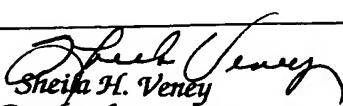
2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

<p>Name and mailing address of the ISA/ US Mail Stop PCT, Attn: ISA/US Commissioner for Patents P.O. Box 1450 Alexandria, Virginia 22313-1450 Facsimile No. (703) 305-3230</p>	<p>Authorized officer  Sundeep S. Virdi Telephone No. 703-308-0858</p>
 Sheila H. Veney Paralegal Specialist Tech. Center 3700	

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International application No.

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Box No. I Basis of this opinion

1. With regard to the language, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

This opinion has been established on the basis of a translation from the original language into the following language _____, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any nucleotide and/or amino acid sequence disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

a. type of material

- a sequence listing
 table(s) related to the sequence listing

b. format of material

- in written format
 in computer readable form

c. time of filing/furnishing

- contained in international application as filed.
 filed together with the international application in computer readable form.
 furnished subsequently to this Authority for the purposes of search.

3. In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

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Box No. V Reasoned statement under Rule 43 bis.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims <u>1-10</u>	YES
	Claims <u>NONE</u>	NO
Inventive step (IS)	Claims <u>NONE</u>	YES
	Claims <u>1-10</u>	NO
Industrial applicability (IA)	Claims <u>1-10</u>	YES
	Claims <u>NONE</u>	NO

2. Citations and explanations:

Please See Continuation Sheet

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

V. 2. Citations and Explanations:

Claims 1-4, 6 and 7 lack an inventive step under PCT Article 33(3) as being obvious over CHEN ET AL in view of DePrince.

Chen discloses a controlled-release drug delivery system comprising an inflexible sleeve (see figure 1) with a first controlled-release layer (10) and a second controlled-release layer (15) where the controlled release layers are disposed with the sleeve (see figure 1) and are spaced apart from one another, defining a drug-retaining region (5) in the space between the controlled-release layers and admit, in a controlled manner, body fluid into the drug retaining region (see column 8, lines 32-37; if the first layer comes in contact with body fluids so will the drug reservoir). Chen further discloses the controlled-release layers undergoing dissolution by exposure to a body fluid with the rate of dissolution effecting a delay of drug release into an ambient environment (column 7, lines 1-10) and where the controlled-release layers control a rate of diffusion of body fluid into and out of the drug-retaining region (column 8, lines 32-37). Chen also discloses an inner surface of the sleeve with a first sealing surface (19) near the first end and a second sealing surface (18) near the second end, a marginal region of the first controlled-release layer (10) abutting the first sealing surface (19; see figure 1) and a marginal region of the second controlled-release layer (15) abutting the second sealing surface (18; see figure 1), at least one dose being disposed in drug delivery region (5), at least a dose of drug being disposed adjacent of the first end of the sleeve outside of drug-retaining region (figure 1), at least a dose of drug being disposed adjacent of the second end of the sleeve outside of drug-retaining region (figure 1).

Chen does not disclose the sleeve that is open at both ends. DePrince et al discloses a controlled release device with a sleeve that is open at both ends (column 5, lines 62-65). The skilled artisan would find it obvious to combine the teachings of Chen et al with DePrince et al in order to make the device as claimed.

Claim 5 lacks an inventive step under PCT Article 33(2) as being obvious over CHEN ET AL in view of DEPRINCE and further in view of GUO ET AL.

Chen and DePrince disclose the claimed invention as discussed above. However, they do not disclose a first cap, with the first cap having an open center, and being received by the first end of a sleeve and abuts a marginal region of a first controlled release layer and a second cap where the second cap has an open center and where the second cap is received by a second end of a sleeve and abuts a marginal region of a second controlled release layer.

Guo et al discloses a first cap (116), with the first cap having an open center (figure 4) and being received by the first end of a sleeve and abuts a marginal region of a controlled release layer and a second cap where the second cap has an open center and where the second cap is received by a second end of a sleeve and abuts a marginal region of a second controlled release layer (paragraph 0057). The skilled artisan would find it obvious to combine the teachings of Chen et al and DePrince with Guo et al.

Claims 8-10 lack an inventive step under PCT Article 33(2) as being obvious over CHEN ET AL in view of DEPRINCE and GUO and further in view of LYLES ET AL.

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Supplemental Box

In case the space in any of the preceding boxes is not sufficient.

Chen, DePrince and Guo disclose the claimed invention as discussed above. However they do not disclose a dose unit of a drug disposed adjacent the first end of a sleeve outside of a drug retaining region and a dose unit of a drug disposed adjacent the second end of a sleeve outside of a drug retaining region wherein the drug contained in the dose unit disposed inside the drug retaining region differ from the drug of at least one of the dose units disposed outside the drug retaining region and wherein the drug of each dose unit disposed outside the drug-retaining is different from one another.

Lyles et al teaches a dose unit of a drug disposed adjacent the first end of a sleeve outside of a drug retaining region and a dose unit of a drug disposed adjacent the second end of a sleeve outside of a drug retaining region wherein the drug contained in the dose unit disposed inside the drug retaining region differ from the drug of at least one of the dose units disposed outside the drug retaining region and wherein the drug of each dose unit disposed outside the drug-retaining is different from one another (column 13, lines 35-50, figure 2). The skilled artisan would find it obvious to combine the teachings of Chen, DePrince and Guo with Lyles et al.

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NOTES TO FORM PCT/ISA/220 (continued)

The letter must indicate the differences between the claims as filed and the claims as amended. It must, in particular, indicate, in connection with each claim appearing in the international application (it being understood that identical indications concerning several claims may be grouped), whether

- (i) the claim is unchanged;
- (ii) the claim is cancelled;
- (iii) the claim is new;
- (iv) the claim replaces one or more claims as filed;
- (v) the claim is the result of the division of a claim as filed.

The following examples illustrate the manner in which amendments must be explained in the accompanying letter:

1. [Where originally there were 48 claims and after amendment of some claims there are 51]:
"Claims 1 to 29, 31, 32, 34, 35, 37 to 48 replaced by amended claims bearing the same numbers;
claims 30, 33 and 36 unchanged; new claims 49 to 51 added."
2. [Where originally there were 15 claims and after amendment of all claims there are 11]:
"Claims 1 to 15 replaced by amended claims 1 to 11."
3. [Where originally there were 14 claims and the amendments consist in cancelling some claims and in adding new claims]:
"Claims 1 to 6 and 14 unchanged; claims 7 to 13 cancelled; new claims 15, 16 and 17 added." or
"Claims 7 to 13 cancelled; new claims 15, 16 and 17 added; all other claims unchanged."
4. [Where various kinds of amendments are made]:
"Claims 1-10 unchanged; claims 11 to 13, 18 and 19 cancelled; claims 14, 15 and 16 replaced by amended
claim 14; claim 17 subdivided into amended claims 15, 16 and 17; new claims 20 and 21 added."

"Statement under Article 19(1)" (Rule 46.4)

The amendments may be accompanied by a statement explaining the amendments and indicating any impact that such amendments might have on the description and the drawings (which cannot be amended under Article 19(1)).

The statement will be published with the international application and the amended claims.

It must be in the language in which the international application is to be published.

It must be brief, not exceeding 500 words if in English or if translated into English.

It should not be confused with and does not replace the letter indicating the differences between the claims as filed and as amended. It must be filed on a separate sheet and must be identified as such by a heading, preferably by using the words "Statement under Article 19(1)."

It may not contain any disparaging comments on the international search report or the relevance of citations contained in that report. Reference to citations, relevant to a given claim, contained in the international search report may be made only in connection with an amendment of that claim.

Consequence if a demand for international preliminary examination has already been filed

If, at the time of filing any amendments and any accompanying statement, under Article 19, a demand for international preliminary examination has already been submitted, the applicant must preferably, at the time of filing the amendments (and any statement) with the International Bureau, also file with the International Preliminary Examining Authority a copy of such amendments (and of any statement) and, where required, a translation of such amendments for the procedure before that Authority (see Rules 55.3(a) and 62.2, first sentence). For further information, see the Notes to the demand form (PCT/IPEA/401).

Consequence with regard to translation of the international application for entry into the national phase

The applicant's attention is drawn to the fact that, upon entry into the national phase, a translation of the claims as amended under Article 19 may have to be furnished to the designated/elected Offices, instead of, or in addition to, the translation of the claims as filed.

For further details on the requirements of each designated/elected Office, see the *PCT Applicant's Guide*, Volume II.

NOTES TO FORM PCT/ISA/220

These Notes are intended to give the basic instructions concerning the filing of amendments under Article 19. The Notes are based on the requirements of the Patent Cooperation Treaty, the Regulations and the Administrative Instructions under that Treaty. In case of discrepancy between these Notes and those requirements, the latter are applicable. For more detailed information, see also the *PCT Applicant's Guide*, a publication of WIPO.

In these Notes, "Article," "Rule" and "Section" refer to the provisions of the PCT, the PCT Regulations and the PCT Administrative Instructions, respectively.

INSTRUCTIONS CONCERNING AMENDMENTS UNDER ARTICLE 19

The applicant has, after having received the international search report, one opportunity to amend the claims of the international application. It should however be emphasized that, since all parts of the international application (claims, description and drawings) may be amended during the international preliminary examination procedure, there is usually no need to file amendments of the claims under Article 19 except where, e.g. the applicant wants the latter to be published for the purposes of provisional protection or has another reason for amending the claims before international publication. Furthermore, it should be emphasized that provisional protection is available in some States only.

What parts of the international application may be amended ?

Under Article 19, only the claims may be amended.

During the international phase, the claims may also be amended (or further amended) under Article 34 before the International Preliminary Examining Authority. The description and drawings may only be amended under Article 34 before the International Preliminary Examining Authority.

Upon entry into the national phase, all parts of the international application may be amended under Article 28 or, where applicable, Article 41.

When ? Within 2 months from the date of transmittal of the international search report or 16 months from the priority date, whichever time limit expires later. It should be noted, however, that the amendments will be considered as having been received on time if they are received by the International Bureau after the expiration of the applicable time limit but before the completion of the technical preparations for international publication (Rule 46.1).

Where not to file the amendments ?

The amendments may only be filed with the International Bureau and not with the receiving Office or the International Searching Authority (Rule 46.2).

Where a demand for international preliminary examination has been/is filed, see below.

How ? Either by cancelling one or more entire claims, by adding one or more new claims or by amending the text of one or more of the claims as filed.

A replacement sheet must be submitted for each sheet of the claims which, on account of an amendment or amendments, differs from the sheet originally filed.

All the claims appearing on a replacement sheet must be numbered in Arabic numerals. Where a claim is cancelled, no renumbering of the other claims is required. In all cases where claims are renumbered, they must be renumbered consecutively (Administrative Instructions, Section 205(b)).

The amendments must be made in the language in which the international application is to be published.

What documents must/may accompany the amendments ?

Letter (Section 205(b)):

The amendments must be submitted with a letter.

The letter will not be published with the international application and the amended claims. It should not be confused with the "Statement under Article 19(1)" (see below, under "Statement under Article 19(1)").

The letter must be in English or French, at the choice of the applicant. However, if the language of the international application is English, the letter must be in English; if the language of the international application is French, the letter must be in French.